

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 09 October 2000 (09.10.00)	
International application No. PCT/US00/00931	Applicant's or agent's file reference 4152-2-PCT
International filing date (day/month/year) 14 January 2000 (14.01.00)	Priority date (day/month/year) 14 January 1999 (14.01.99)
Applicant COX, George, N. et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

15 August 2000 (15.08.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☐ was

☒ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer R. E. Stoffel Telephone No.: (41-22) 338.83.38
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PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE
in its capacity as elected Office

Date of mailing (day/month/year) 12 November 2001 (12.11.01)	
International application No. PCT/US00/00931	Applicant's or agent's file reference 4152-2-PCT
International filing date (day/month/year) 14 January 2000 (14.01.00)	Priority date (day/month/year) 14 January 1999 (14.01.99)
Applicant COX, George, N. et al	

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☒ in the demand filed with the International Preliminary Examining Authority on:
14 August 2000 (14.08.00)

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☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

CORRECTED
VERSION

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer François BAECHELER Telephone No.: (41-22) 338.83.38
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/00931

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 15/00, 15/20; C07K 17/08, 14/555, 14/475

US CL : 435/69.51, 471, 252.3, 252.8, 255.1; 530/402, 351

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/69.51, 471, 252.3, 252.8, 255.1; 530/402, 351

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	WO 95/32003 A1 (AMGEN BOULDER INC.) 30 Novmeber 1995 (30.11.95), especially see, page 6, lines 2-10, page 24, lines 7-30, page 29, lines 28-30 and claims 1, 2.	1-9, 15-16, 18-19, 26, 29-31 ----- 10-14, 17, 20-25, 27-28
X --- Y	US 5,766,897 A (BRAXTON) 16 June 1998 (16.06.98), see especially abstract and column 11, lines 39-65, column 12 lines 1-6, table 1A on column 12, column 37, lines 1-5, and column 47, lines 3-14.	1-13, 15, 18-19, 26-31 ----- 14, 16-17, 20-25

☒ Further documents are listed in the continuation of Box C.
 ☐ See patent family annex.

* Special categories of cited documents:	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
A document defining the general state of the art which is not considered to be of particular relevance	*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
E earlier document published on or after the international filing date	*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*g* document member of the same patent family
O document referring to an oral disclosure, use, exhibition or other means	
P document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search 15 MARCH 2000	Date of mailing of the international search report 26 APR 2000
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer <i>FOZIA HAMUD</i> Telephone No. (703) 308-0196

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/00931

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ---- Y	US 5,206,344 A (KATRE et al.) 27 April 1993 (27.04.93), see especially abstract and column 12, lines 50-68, Example 1 on column 16, claims 1, 9.	1-8, 15-16, 18-19, 26, 29-31 ----- 9-14, 17, 20-25, 27-28

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/00931

B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

East, US pat full; STN via medline, caplus, embase; search terms: cysteine muteins, free cysteine; (gluthione, cystine, pyridine disulfides, cysteine blocking agents), PEG or polyethylene glycol,

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PATENT COOPERATION TREATY

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REC'D 22 JUN 2001

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

PCT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 4152-2-PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US00/00931	International filing date (day/month/year) 14 JANUARY 2000	Priority date (day/month/year) 14 JANUARY 1999
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.		
Applicant BOLDER BIOTECHNOLOGY INC.		

- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 4 sheets.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of _____ sheets.

- This report contains indications relating to the following items:
 - ☒ Basis of the report
 - ☐ Priority
 - ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
 - ☐ Lack of unity of invention
 - ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
 - ☐ Certain documents cited
 - ☐ Certain defects in the international application
 - ☐ Certain observations on the international application

Date of submission of the demand 15 AUGUST 2000	Date of completion of this report 09 MAY 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer <i>Olga Chernyshev</i> OLGA CHERNYSHEV
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/00931

I. Basis of the report

1. With regard to the elements of the international application:*

☒ the international application as originally filed

☒ the description:

pages 1-77

pages NONE, as originally filed

pages NONE, filed with the demand

pages NONE, filed with the letter of

☒ the claims:

pages 78-80

pages NONE, as originally filed

pages NONE, as amended (together with any statement) under Article 19

pages NONE, filed with the demand

pages NONE, filed with the letter of

☒ the drawings:

pages NONE

pages NONE, as originally filed

pages NONE, filed with the demand

pages NONE, filed with the letter of

☒ the sequence listing part of the description:

pages NONE

pages NONE, as originally filed

pages NONE, filed with the demand

pages NONE, filed with the letter of

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

☒ the description, pages NONE

☒ the claims, Nos. NONE

☒ the drawings, sheets/fig. NONE

5. ☐ This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/00931

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement**1. statement**

Novelty (N)	Claims	<u>14, 17, 20-25</u>	YES
	Claims	<u>1-13, 15-16, 18-19, 26-31</u>	NO
Inventive Step (IS)	Claims	<u>NONE</u>	YES
	Claims	<u>1-31</u>	NO
Industrial Applicability (IA)	Claims	<u>1-31</u>	YES
	Claims	<u>NONE</u>	NO

2. citations and explanations (Rule 70.7)

Claims 1-13, 15, 18-19, 26-31 lack novelty under PCT Article 33(2) as being anticipated by BRAXTON.

BRAXTON discloses methods and compositions for the production of soluble proteins having a free cysteine. The list of these proteins, referred to as cysteine-PEGylated proteins, includes any protein, protein fragment, or peptide having biological activity for which increased biological stability is desired (see especially abstract, column 11 lines 39-65, column 12 lines 1-6, Table 1A on column 12). Also disclosed are cysteine blocking agents and compounds (see column 37 lines 1-8). The method of formation of cysteine modified proteins by attaching a polyethylene glycol to form a pegylated protein is taught (see column 47 lines 3-14, for example).

Claim 16 lacks novelty under PCT Article 33(2) as being anticipated by AMGEN BOULDER INC..

AMGEN BOULDER INC. discloses an invention directed to PEG conjugates attached to the free cysteine through a thiol-specific activating group, examples given (see page 6 lines 2-10, and claim 2).

Claims 14 lacks an inventive step under PCT Article 33(3) as being obvious over BRAXTON. BRAXTON discloses methods and compositions for production of modified stable cysteine-pegylated proteins, muteins and conjugates of proteins. BRAXTON does not disclose cysteine muteins of a heavy or light chain of an immunoglobulin or derivative thereof. However, it would have been obvious to a person having ordinary skill in the art to use the method of BRAXTON for obtaining of cysteine muteins of heavy or light chain of an immunoglobulin or derivative thereof because BRAXTON teaches his method for obtaining any protein, protein fragment or peptide having biological activity for which increased biological stability is desired (see column 11 lines 39-65, column 12 lines 1-6), and this would be desirable for immunoglobulins.

(Continued on Supplemental Sheet.)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/00931

Supplemental B x

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below:
IPC(7): C12N 15/00, 15/20; C07K 17/08, 14/555, 14/475 and US Cl.: 435/69.51, 471, 252.3, 252.8, 255.1; 530/402, 351

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):

Claim 17 lacks an inventive step under PCT Article 33(3) as being obvious over AMGEN BOULDER INC.. AMGEN BOULDER INC. teach thiol-reactive compounds as cysteine blocking agents. AMGEN BOULDER INC. do not disclose cystine as a suitable compound. However, it would have been obvious to a person of ordinary skill in the art to follow the protocol of AMGEN BOULDER INC. and use cystine as a cysteine blocking agent because cystine belongs to a group of thiol-specific activating compounds.

Claims 20-25 lack an inventive step under PCT Article 33(3) as being obvious over BRAXTON. BRAXTON teaches the methods and compositions for the production of PEGylated proteins. BRAXTON does not teach proteins of specific molecular weights or specific locations of attached PEG moiety. However, it would have been obvious to a person having ordinary skill in the art to practice the invention of Braxton for any protein or a derivative thereof or to attach the PEG moiety to the desirable protein.

____ NEW CITATIONS _____

NONE